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Sinus Node Function After Cardiac Transplantation

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Objectives. **This study aimed to examine changes over time in sinus node function after cardiac transplantation; to determine the incidence, natural history and etiology of sinus node dysfunction in transplant recipients; and to identify any early predictors of long-term sinus node function.**

Background. **Bradyarrhythmias caused by sinus node dysfunction are common immediately after cardiac transplantation. Existing electrophysiologic studies have been limited by small numbers and have reported an unexpectedly high incidence of sinus node dysfunction (~50%) compared with the incidence of bradyarrhythmias in other studies. There have been no previous studies reporting serial electrophysiologic data. Thus, the natural history of sinus node dysfunction after transplantation has not been adequately described.**

Methods. **Serial electrophysiologic studies of sinus node function and 24-h ambulatory electrocardiographic recordings were performed at 1, 2, 3 and 6 weeks and 3 and 6 months after transplantation in 40 adult recipients.**

Results. **The overall incidence of sinus node dysfunction was 17.5% (7 of 40). Six patients (15%) had sinus node dysfunction from week 1; one developed sinus node dysfunction at 3 months. Sinus node recovery time returned to normal by 6 weeks in all six patients with early sinus node dysfunction, but abnormalities of sinoatrial conduction persisted in two. Two patients who required pacing during ambulatory monitoring at 2 weeks after transplantation (temporary pacemaker 50 beats/min, demand) received a permanent pacemaker. One patient required pacing at 3 weeks and continued to require pacing 6 months after transplantation.**

Conclusions. **The incidence of sinus node dysfunction after cardiac transplantation is lower than has been previously reported in electrophysiologic studies. Sinus node automaticity improves with time, although abnormalities of sinoatrial conduction may persist. The best predictor of permanent pacing requirements is the temporary pacing requirements during 24-h Holter monitoring 2 and 3 weeks after transplantation, with temporary pacing set at 50 beats/min on demand.**

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Bradycardia is common immediately after cardiac transplantation (1–3). Although atrioventricular (AV) block does occur, bradyarrhythmias of sinus node origin predominate (3). Sinus bradycardia, nodal bradycardia and sinus arrest remain common throughout the first few days and are usually managed by temporary pacing (3). The proportion of transplant recipients receiving permanent pacemakers for persistent sinus node dysfunction varies considerably from center to center. Implantation rates between 4% and 29% have been reported (3–7). This variation may reflect differences in both the incidence of bradyarrhythmias and the criteria for permanent pacing.

In previous studies of transplant recipients, sinus node dysfunction has been defined primarily by electrophysiologic techniques. Electrophysiologic studies have been undertaken both in recent transplant recipients (8–10) and in long-term survivors (11). However, with the exception of a small study limited to permanent pacemaker recipients (12), serial electrophysiologic data have not been reported. There have also been no previous studies in which sinus node function after transplantation has been systematically evaluated by ambulatory monitoring. Thus, the natural history of sinus node dysfunction after transplantation has not been adequately described. Our previous findings (7,13) that patients who received permanent pacemakers infrequently require long-term pacing suggest that early sinus node dysfunction resolves.

The incidence of early sinus node dysfunction reported in existing electrophysiologic studies (8–10) is ~50%. In all these studies clinically significant bradyarrhythmias were also common. The much lower incidence of clinical bradyarrhythmias reported in a substantially larger series (3) suggests that existing studies may have overestimated the frequency of sinus node dysfunction.

The aims of this study were to examine changes over time in sinus node function after transplantation; to determine the incidence, natural history and etiology of sinus node dysfunction in transplant recipients; and to identify any potential predictors of long-term sinus node function. These data have obvious implications for the appropriate prescription of permanent pacing systems.

Methods

Patients. All 44 adults who underwent transplantation at this center between October 1991 and January 1993 were

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considered for inclusion in the study. One patient refused consent, and three were excluded. Two of the three did not survive the first postoperative week, and one required prolonged intensive care. Forty cardiac transplant recipients were therefore recruited.

All underwent orthotopic transplantation using the standard atrial anastomosis technique described by Lower et al. (14). The donor heart was perfused and topically cooled with St. Thomas's cardioplegia solution at 4°C. Temporary epicardial pacing wires were inserted at the time of transplantation and removed 3 weeks after operation. Two pairs were attached to the donor atrium and one pair to the ventricle. The spontaneous cardiac rhythm was recorded immediately after defibrillation, after weaning from cardiopulmonary bypass and on return to the intensive care unit.

Endomyocardial biopsies were performed routinely at weekly intervals for 6 weeks, 2-weekly until 12 weeks, monthly until 6 months and 3-monthly thereafter and at other times if there was clinical suspicion of rejection. Biopsies were histologically graded using the Billingham classification (15).

Immunosuppression was achieved with cyclosporine, azathioprine and prednisolone. Additional potentially cardioactive drugs were prescribed for noncardiac indications in six patients. Anticonvulsant agents were required in four patients: carbamazepine in one, phenytoin in two; both were used at different times in another patient. Diltiazem was prescribed for hypertension in five patients. No patient received beta-adrenergic blocking agents.

All patients gave informed written consent, and all investigations were approved by the joint ethical committee of the University of Newcastle upon Tyne and Newcastle District Health Authority.

Pacing protocol. Temporary atrial pacing was used where necessary in the immediate postoperative period to maintain a heart rate of at least 100 beats/min. This was continued for up to 21 days in some patients to maintain a heart rate of at least 50 beats/min. A higher temporary pacing (90 beats/min) rate was used if clinically indicated during the first week. Those who required pacing 3 weeks after transplantation had a permanent pacemaker implanted. A requirement for pacing was defined by the occurrence of symptomatic bradyarrhythmias during normal activity or symptomatic chronotropic incompetence on exercise testing after withdrawal of temporary pacing.

Electrophysiologic studies. Electrophysiologic studies were performed in each patient 1, 2, 3 and 6 weeks and 3 and 6 months after transplantation. All subjects were studied in the supine position after resting for at least 30 min. Temporary cardiac pacing was discontinued at least 10 min before each study.

The surface electrocardiogram (ECG) was recorded throughout the study (leads I and V_1). The first three electrophysiologic studies were performed using temporary epicardial pacing wires. The remaining studies were carried out at the time of surveillance endomyocardial biopsies. An atrial "J" quadripolar electrode catheter (Bard Electrophysiology) was inserted through the right internal jugular vein and placed in the donor atrium. Its position was confirmed by fluoroscopy and by simultaneous monitoring of the surface ECG and atrial electrograms.

All studies were performed with a programmed stimulator delivering a constant square voltage waveform of 2-ms duration at twice diastolic threshold. Intracardiac electrograms and surface ECG signals were recorded with a Gould electrostatic recorder at a paper speed of 100 mm/s. All measurements were made from intracardiac electrograms to an accuracy of 5 ms.

The spontaneous cycle length was calculated from an average of 10 cardiac cycles before any pacing. Sinus node recovery time was assessed by overdrive pacing of the donor atrium for 30 s at varying cycle lengths and measuring the interval between the last paced and the first spontaneous sinus beats. The identical origin of sinus beats before and after recovery time pacing sequences was verified by comparison of P wave configuration. Decremental cycle lengths at 100-ms intervals were used, starting just below the spontaneous sinus rate to a minimum of 400 ms. At least 1 min elapsed between pacing sequences. The corrected sinus node recovery time was calculated by subtracting the spontaneous cycle length from the sinus node recovery time. Sinoatrial conduction time was measured using the single atrial extrastimulus technique (16). Secondary pauses were defined as any being present when any recovery sinus cycle was longer than the primary recovery cycle (17).

Ambulatory monitoring. Twenty-four hour Holter ECG recordings were planned on six occasions for each of 40 subjects at 1, 2, 3 and 6 weeks and 3 and 6 months after transplantation. Ambulatory recordings (Reynolds Medical, Tracker) were performed to assess the incidence of bradyarrhythmias and were therefore omitted when patients were continuously paced. Recordings were also omitted during acute complications likely to distort heart rate data (e.g., pyrexial illness).

All recordings were analyzed using the Reynolds Medical Pathfinder 3 analyzer. The minimal heart rate and minimal daytime heart rate were determined automatically by the analyzer using 2-min sample periods and were individually verified by direct inspection. The mean heart rate over 24 h was calculated from automated QRS counts provided that the recording was of sufficient quality. Sinus pauses >2 and any pacemaker activity were individually documented.

Statistical methods. Statistical analyses were performed using an IBM-compatible computer and Minitab (version 7.0, 1989, Minitab Inc.) and Statgraphics (version 2.6, STSC Inc.) statistical software.

Changes in sinus node function variables over time were analyzed by two-way analysis of variance on subjects and times. Patients with >50% of intended observations missing were excluded. Isolated missing electrophysiologic data were estimated using the Minitab Generalized Linear Model command function. Fisher exact and chi-square tests were used to examine the relation between sinus node dysfunction and rejection, perioperative rhythm and subsequent mortality. Changes in heart rate over time were analyzed using one-way

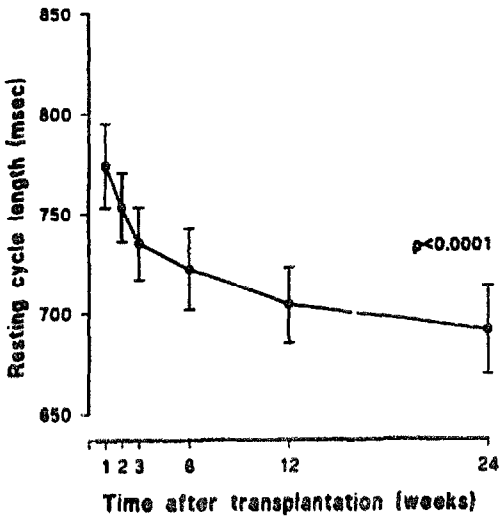

Figure 1. Changes in sinus cycle length over time after transplantation. **Bars** represent standard error. Statistical analysis was by two-way analysis of variance.

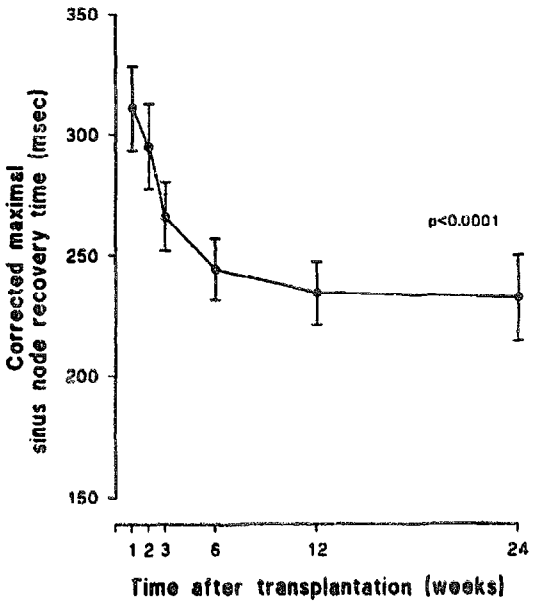

Figure 2. Changes in corrected maximal sinus node recovery time over time after transplantation. **Bars** represent standard error. Statistical analysis was by two-way analysis of variance.

analysis of variance. The associations between electrophysiologic measurements of sinus node function, heart rate and donor and recipient ages and perioperative ischemic time were assessed by linear correlation analysis.

Results

Thirty-six patients (90%) were male. The indication for transplantation was ischemic heart disease in 20 patients, dilated cardiomyopathy in 17, congenital heart disease in 2 and valvular disease in 1. The mean (±SD) recipient and donor ages were 46.6 ± 11.8 and 35.3 ± 10.5 years, respectively.

Electrophysiologic studies. *Sinus node function.* In 33 (82.5%) of 40 patients, sinus node function remained within the normal range (corrected maximal sinus node recovery time <525 ms and sinoatrial conduction time <250 ms [18]) for the duration of the study. The analyses in this section are restricted to these 33 subjects.

A progressive decrease in mean rest cycle length over time was observed after transplantation (Fig. 1). There was no change in P wave configuration. Individual changes in rest cycle length were variable. Between 1 week and 6 months, the cycle length decreased in 23 (82%) of 28 patients and increased in 5 (18%). The initial rest cycle length was <700 ms in all five patients in whom it subsequently increased. The overall mean cycle length at 6 months was 695 ms.

Corrected maximal sinus node recovery time also decreased significantly with time after transplantation ($p < 0.0001$). Figure 2 illustrates the changes in overall mean corrected maximal sinus node recovery time. However, the individual changes varied considerably. In general, those patients with initially short sinus node recovery times (<200 ms) exhibited no change or had small increases, whereas the remainder had significant decreases. One-week and 6-month electrophysiologic data were both available for 28 of 33 patients. Corrected maximal sinus node recovery time decreased in 20 (71%) subjects and increased in 8 (29%).

The sinoatrial conduction time was within normal limits throughout the study in all 33 patients with consistently normal corrected maximal sinus node recovery time. There was a significant change with time after transplantation ($p = 0.02$) (Fig. 3). Unlike the other indexes of sinus node function, where a smooth progression over time was observed, the change occurred abruptly between 3 and 6 weeks. The mean sinoatrial conduction time during the first 3 weeks was 153 ± 38 ms compared with 138 ± 40 ms during later measurements ($p = 0.017$, paired t test).

Figure 3. Changes in sinoatrial conduction time over time after transplantation. **Bars** represent standard error. Statistical analysis was by two-way analysis of variance.

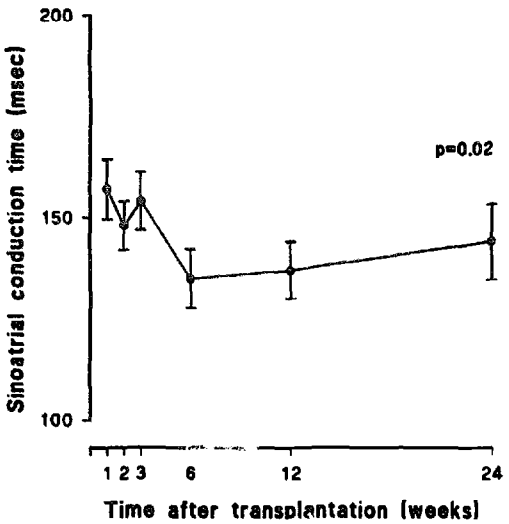

Table 1. Electrophysiologic Results in Patients With Abnormal Sinus Node Function

Pt No./Gender	Wk 1	Wk 2	Wk 3	Wk 6	Mo 3	Mo 6
14/M						
$CSNRT_{max}$	Nodal	675	460	315	230	255
SACT	Nodal	270	256	133	145	186
Cycle length	1,395	715	680	610	660	685
15/M						
$CSNRT_{max}$	Nodal	1,430	565	405	280	265
SACT	Nodal	312	294	235	200	109
Cycle length	1,070	790	870	800	775	810
16/M						
$CSNRT_{max}$	260	255	235	365	1,825	1,460
SACT	80	110	116	4	75	126
Cycle length	1,020	945	885	970	955	685
19/F						
$CSNRT_{max}$	1,350	—	—	—	—	—
SACT	226	—	—	—	—	—
Cycle length	800	—	—	—	—	—
21/M						
$CSNRT_{max}$	535	—	—	—	—	—
SACT	255	—	—	—	—	—
Cycle length	725	—	—	—	—	—
33/M						
$CSNRT_{max}$	795	2,385	1,325	485	445	450
SACT	159	—	197	243	271	269
Cycle length	1,165	1,220	950	745	810	710
37/M						
$CSNRT_{max}$	575	450	345	400	290	385
SACT	298	334	249	199	163	295
SCL	770	705	705	720	730	800

All measurements are in milliseconds; $CSNRT_{max}$ = corrected maximal sinus node recovery time; Cycle length = spontaneous rest cycle length; Pt = patient; SACT = sinoatrial conduction time.

Sinus node dysfunction. Corrected maximal sinus node recovery time was abnormal by standard criteria (>525 ms) on at least one occasion in 7 (17.5%) of 40 patients. The electrophysiologic data are detailed in Table 1. Six of the seven patients had an abnormally prolonged corrected maximal sinus node recovery time at 1 week (early sinus node dysfunction) that returned to normal in all four survivors by the sixth postoperative week. No increase in sinus node recovery time was observed after the second week. One patient first had an abnormal corrected maximal sinus node recovery time 3 months after operation (late sinus node dysfunction). Prolonged secondary pauses accompanied measurements of recovery time in this patient from the first week. Secondary pauses were not recorded in any other patient with normal sinus node recovery times.

Sinoatrial conduction times were abnormal by standard criteria (>250 ms) on 10 occasions in five patients. All five had abnormal sinus node recovery time early after transplantation. In five studies in three patients, an abnormal sinoatrial conduction time was associated with a normal corrected maximal sinus node recovery time. Six months after transplantation, two (50%) of four patients with early sinus node dysfunction had abnormal sinoatrial conduction despite a return to normal of corrected maximal sinus node recovery time. An unusually short sinoatrial conduction time of 4 ms was recorded in one patient 6 weeks after transplantation.

Sinus node function and rest cycle length. The changes in mean rest cycle length in patients both with and without sinus node dysfunction closely parallel changes in mean corrected maximal sinus node recovery times. However, rest sinus cycle length is not a reliable predictor of sinus node recovery time in individual patients, particularly in the first 3 weeks. For example, the range of corrected maximal sinus node recovery times for a rest cycle length of 700 to 800 ms was between 140 and 1,430 ms. Linear correlation analysis reveals coefficients of between 0.34 and 0.42 (r^2 12% to 18%) in the first 3 weeks and between 0.63 and 0.72 (r^2 40% to 52%) between 6 weeks and 6 months.

Complications and associations. Two of 7 patients with sinus node dysfunction died during the study period compared with 3 of 33 other patients. This difference was not statistically significant ($p = 0.2$), and none of the deaths was attributable to arrhythmias.

Allograft rejection was not associated with sinus node dysfunction. Two of seven patients with sinus node dysfunction had significant (moderate) rejection during the study period compared with 8 of 33 with normal sinus node function ($p = 0.57$).

Table 2. Perioperative Rhythm and Subsequent Sinus Node Dysfunction

	Normal SN Function (n = 33)		Subsequent SND (n = 7)		
Stage	Sinus	Other	Sinus	Other	p Value
Defibrillation	16 (48%)	17 (52%)	4 (47%)	3 (43%)	0.50
Off bypass	25 (76%)	8 (24%)	2 (29%)	5 (71%)	0.03
ITU	28 (85%)	5 (15%)	4 (57%)	3 (43%)	0.13

Data presented are number (%) of subjects. Defibrillation = immediately after implantation and defibrillation of the transplanted heart; ITU = after return to intensive care unit; Off bypass = after weaning from cardiopulmonary bypass; SN = sinus node; SND = sinus node dysfunction.

There was no association between operative ischemic time and subsequent sinus node function. The ischemic time was 182 ± 51 min in those recipients with sinus node dysfunction compared with 179 ± 52 min in the remainder (p = 0.91). There were no relations between donor or recipient ages and subsequent sinus node dysfunction. The donor and recipient ages were, respectively, 31 ± 7 and 47 ± 13 years in those patients with sinus node dysfunction and 36 ± 11 and 46 ± 12 years in the remainder (p = 0.2 and p = 0.88).

The spontaneous cardiac rhythms recorded in the immediate postoperative period and their relation to subsequent sinus node dysfunction are summarized in Table 2. The rhythm after weaning from cardiopulmonary bypass appeared to be predictive of subsequent sinus node function. However, both the positive and negative predictive accuracy of this observation at 71% and 76%, respectively, are poor.

Ambulatory monitoring. At the time of proposed ambulatory monitoring 1 week after transplantation, continuous temporary pacing at 90 beats/min was judged clinically necessary in eight patients, and ambulatory recordings were therefore omitted. A total of 14 recordings were lost because of the deaths of five patients, two of whom died before undergoing any ambulatory monitoring. Thirty-eight recordings were unavailable because patients refused ambulatory monitoring at that time or had developed acute complications. Of the remaining 185 recordings, 166 (90%) were suitable for analysis; 19 were lost through technical failures or were of insufficient quality; 134 (81% of those analyzed) were suitable for calculation of mean heart rate.

Minimal and mean heart rates. Paced heart rates are not included in the following analyses. The changes in overall minimal, daytime minimal and mean heart rates over time after transplantation are summarized in Table 3. There was a trend toward higher mean heart rates with increasing time after transplantation, but this was not statistically significant. No sinus pauses ≥2 s were observed during any recording.

The exclusion of five patients with electrophysiologic evidence of sinus node dysfunction on at least one occasion did not affect these analyses. These patients frequently required temporary pacing in the first few weeks and were therefore omitted from the previous analyses. Sinus node dysfunction had usually resolved by the time of subsequent ambulatory monitoring.

Bradyarrhythmias and temporary and permanent pacing. One week after transplantation, eight patients (20%) were clinically judged to require temporary pacing at 90 beats/min. On ambulatory monitoring, six patients (15%) required intermittent pacing at 50 beats/min, three of whom had abnormal sinus node electrophysiology. One patient with an abnormal corrected maximal sinus node recovery time (575 ms) at 1 week maintained sinus rhythm at a minimal rate of 72 beats/min throughout 24 h of ambulatory monitoring. Ambulatory recordings were not available for two patients with sinus node dysfunction who died in the second week.

Two weeks after transplantation only two patients (Patients 15 and 33) required pacing during 24 h of ambulatory monitoring. Both had abnormal corrected maximal sinus node recovery times (1,430 and 2,385 ms, respectively). At 3 weeks, only Patient 33 required pacing during ambulatory monitoring and had an abnormal corrected maximal sinus node recovery time (1,325 ms). Patient 15 had a minimal heart rate of 55 beats/min during 24-h ambulatory monitoring, but his exercise capacity was severely limited by presyncope, which was corrected by atrial pacing at 100 beats/min. Both patients received rate-adaptive physiologic permanent pacemakers 22 and 24 days after transplantation. They represent 5% of the study group overall and 29% of those with sinus node dysfunction. An abnormal corrected maximal sinus node recovery time in the first 3 weeks after transplantation predicted subsequent pacing with a sensitivity of 100% but a specificity of only 33% (positive predictive value 33%, negative predictive value

Table 3. Heart Rates (beats/min) During Ambulatory Monitoring

Heart Rate	Wk 1	Wk 2	Wk 3	Wk 6	Mo 3	Mo 6
Minimal	70 ± 2.4	69 ± 2.1	71 ± 2	73 ± 2.1	72 ± 2.5	72 ± 2.9
Minimal daytime	76 ± 2.4	74 ± 2.1	77 ± 2	79 ± 2.4	80 ± 2.3	76 ± 2.6
Mean	79 ± 2.2	79 ± 2.2	80 ± 1.8	83 ± 2.3	88 ± 2.9	84 ± 2.7

Data presented are mean value ± SD.

100%). Abnormal sinus node recovery at 3 weeks had both 100% sensitivity and specificity.

Patient 15 had normal sinus node function by electrophysiologic criteria for the remainder of the study, and the minimal heart rate during subsequent ambulatory monitoring was 57 beats/min. He was able to exercise normally from the sixth week without requiring pacing. Patient 33 required pacing intermittently at 6 weeks, no pacing at 3 months and pacing again 6 months after transplantation. Sinus node recovery time was normal from the sixth week, but the sinoatrial conduction time was abnormal at 3 and 6 months after transplantation.

The patient who developed late sinus node dysfunction (Patient 16) had a minimal heart rate of 54 beats/min during ambulatory monitoring.

Discussion

Electrophysiology. *Sinus node electrophysiology.* This study demonstrates that among those patients with normal sinus node function by standard criteria, there is a significant shortening over time of mean sinus node recovery time after transplantation. This observation has not been previously reported. No subject with normal sinus node function experienced significant bradyarrhythmias; thus, the clinical relevance of the decrease in sinus node recovery times is unknown. However, it does illustrate that there is relative impairment of sinus node automaticity in some patients in the immediate postoperative period.

The change in mean sinoatrial conduction time between the early (1 to 3 weeks) and later studies coincided with the change from recording of epicardial to endocardial electrograms. This is not a surprising finding. Of all the indexes of sinus node function, the sinoatrial conduction time would be expected to be most sensitive to the distance between the recording and stimulating electrodes and the sinus node. From the results of this study epicardial pacing and recording produces sinoatrial conduction times ~10% longer than the use of endocardial electrodes.

There is a progressive decrease in rest sinus cycle length with time after transplantation. It is well recognized that relative bradycardia is usual in transplant recipients immediately after operation (1,2) and that tachycardia is usual in long-term survivors (19,20). This study describes the time course of the changes in rest heart rate over the first 6 months. A possible explanation for these changes and those in sinus node automaticity is the effect of acute sympathetic denervation at the time of transplantation and subsequent development of presynaptic catecholamine supersensitivity (21).

An unusually short sinoatrial conduction time such as that observed on one occasion in this study (4 ms) has been reported previously (22). Various potential causes for this phenomenon were suggested, including pacemaker shift and sinus node reentry. Whatever mechanism is involved, it appears to have been transient because the phenomenon was not observed during subsequent studies in our subject.

In standard therapeutic doses, potentially cardioactive drugs commonly used in transplant recipients (carbamazepine, phenytoin and diltiazem) did not significantly affect sinus node function. This is in keeping with previous studies of the electrophysiologic actions of these agents (23–25), which have reported no consistent changes in the indexes of sinus node function.

Sinus node dysfunction. The 15% frequency of early sinus node dysfunction in this study is substantially lower than the previously reported incidences of 44% to 50% (8–10). Two of these studies involved substantially fewer patients (8,10). Heinz et al. (9) studied 90 transplant recipients, but they also consistently reported unusually high rates of symptomatic bradyarrhythmias (5) and subsequent pacemaker implantation compared with other large centers (3,6,7). Immunosuppression and organ preservation protocols are similar. It therefore seems likely that local differences in surgical technique may be responsible for an unusually high incidence of sinus node dysfunction reported by this group (9).

We believe that this is the first study to undertake systematic serial electrophysiologic measurements of sinus node function from the early posttransplant period to 6 months. The improvement in sinus node recovery observed in the current study is in keeping with several previous reports (3,5,7,13) in which subsequent pacing independence was observed in up to 75% of patients who initially required permanent pacing for sinus node dysfunction. Heinz et al. (12) reported a single follow-up electrophysiologic study in eight patients who required pacing for sinus node dysfunction. The results are at variance with the current study: Seven of eight patients had persistent abnormalities of sinus node recovery time compared with none of four in the current study. Sinoatrial conduction was not measured. The subsequent development of abnormalities of sinoatrial conduction in 50% of patients with early abnormalities of sinus node automaticity in this study has not been previously reported.

Sinus node dysfunction and mortality. Sinus node dysfunction was not, as has been previously stated (8), a cause of increased mortality in this study. The only deaths reported in published data due to bradyarrhythmias after transplantation are one of the four deaths reported by Mackintosh et al. (8) and one reported by Grinstead et al. (26). In each case the terminal rhythm was AV block and was associated with moderate rejection and severe graft coronary artery disease, respectively.

Late sinus node dysfunction. The low observed frequency of late sinus node dysfunction (2.5%) in this study contrasts with a much higher frequency (4 [29%] of 14 patients) in the small study by Bexton et al. (11). The frequency of late bradyarrhythmias requiring permanent pacing in other large series (3,6) has been low, but sinus node dysfunction in the absence of clinical symptoms would not have been identified and may have been more frequent.

Ambulatory monitoring. *Heart rates.* The absence of any clear trend toward higher mean and minimal heart rates with increasing time after transplantation is surprising in view of the trends in rest cycle length during electrophysiologic studies.

This is probably explained by the necessary elimination of paced heart rates from the analysis (mostly in the first week).

Two previous studies have measured mean heart rate in transplant recipients by ambulatory monitoring techniques. Heinz et al. (9) reported a mean heart rate of 94.2 ± 9 beats/min in 51 patients 3 months after transplantation. Alexopoulos et al. (19) reported a mean rate of 99 ± 11 beats/min in 19 patients between 6 months and 3 years after transplantation. In comparison, the mean heart rates found in the current study are lower.

Bradyarrhythmias, sinus node dysfunction and pacing requirements. In this study ambulatory monitoring was not helpful in the first week after transplantation. After the first week the results may be more significant, although caution is required in view of the small number of patients with bradyarrhythmias. In this study both patients who required intermittent or continuous pacing at 2 weeks subsequently required permanent pacemakers, and the patient who required intermittent pacing at 3 weeks continued to require intermittent long-term pacing.

There have been no previous studies using ambulatory ECG monitoring early after transplantation to assess the need for permanent pacing. Two groups have published the results of ambulatory monitoring in long-term transplant survivors. Bexton et al. (11) reported "relative bradycardia" in three of four patients with electrophysiologic evidence of sinus node dysfunction between 4 and 14 months after transplantation. Two of these patients had ventricular pacemakers programmed to 70 beats/min; the other had a minimal recorded heart rate of 57 beats/min. Heinz et al. (9) reported that 44% of patients with early sinus node dysfunction (corrected maximal sinus node recovery time >520 ms) had ambulatory ECG evidence of persistent sinus node dysfunction 3 months after transplantation. However, the definitions of sinus node dysfunction used were not standard. Permanent pacemakers had been implanted in some patients, and the definition of normal sinus node function included a 24-h mean heart rate of at least 80 beats/min. In the current study two patients who were completely asymptomatic with consistently normal electrophysiologic indexes of sinus node function would have been classified as having sinus node dysfunction by these criteria. Six (35%) of 17 patients defined as having ambulatory ECG evidence of sinus node dysfunction were asymptomatic.

The selection of a relatively low temporary pacing rate of 50 beats/min during early ambulatory monitoring in the current study was essential to identify patients with relative bradycardia but no clinically significant arrhythmias. Although this rate may be disadvantageous to some patients in the first week, all were able to tolerate it from the second week with no ill effects.

Etiology of sinus node dysfunction after transplantation. In this study donor and recipient ages and allograft rejection were not found to influence sinus node function. We have not confirmed the association reported by Heinz et al. (5) between transient sinus node dysfunction and prolonged perioperative ischemia. A low myocardial temperature during the perioperative ischemic period has been reported to be a cause of sinus node dysfunction (27). However, these findings have not been reproduced by other groups. Historical controls and crude measures of sinus node function were used. The most likely cause of sinus node dysfunction after transplantation remains direct surgical trauma or associated disruption of blood supply to the sinus node, or both (6).

Conclusions. The incidence of sinus node dysfunction after cardiac transplantation at this center is lower than has been previously reported by other centers. The prognosis for recovery of normal sinus node automaticity is good. However, associated abnormalities of sinoatrial conduction may persist or develop later. Serial measurements of corrected sinus node recovery time may be useful in the first 3 weeks after transplantation. A decreasing sinus node recovery time during the second and third weeks probably indicates a good prognosis for recovery of sinus node function. The rest sinus cycle length is not a reliable substitute indicator. No specific etiologic factors for early sinus node dysfunction were identified. Among patients with normal sinus node function by standard criteria, there is a decrease over time in mean corrected maximal sinus node recovery time after transplantation, suggesting relative impairment of sinus node automaticity in the immediate postoperative period.

Ambulatory ECG monitoring may be useful in assessing the need for permanent pacing in transplant recipients between 2 and 3 weeks after transplantation. Patients who require continuous or intermittent pacing 3 weeks after transplantation may require long-term pacing. It is essential that temporary pacing rates be set low (50 beats/min) to distinguish patients who may require pacemakers from those with relative but clinically insignificant bradycardia. However, these data should be interpreted with caution in view of the small numbers of patients with clinically important bradyarrhythmias in this study.

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